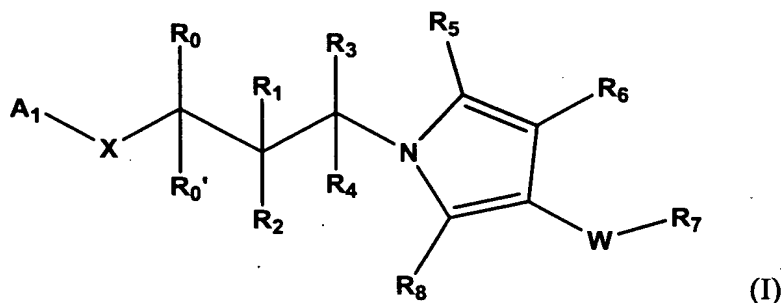


The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A compound having the structure:



wherein:

X is nitrogen, oxygen, or optionally substituted carbon;

W is absent or is selected from the group consisting of -O-, -S-, -S(O)-, -SO<sub>2</sub>-, -NH-, -NH-CO-, -NR'CO-, -NHSO<sub>2</sub>-, -NR'SO<sub>2</sub>-, -CO-, -CO<sub>2</sub>-, -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -CONH-, -CONR'-, and -NR'-, where R' is alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, heterocyclo;

A<sub>1</sub> is optionally substituted aryl or heteroaryl;

R<sub>0</sub> and R<sub>0</sub>' are independently selected from the group consisting of hydrogen and methyl;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are independently selected from the group consisting of hydrogen, hydroxyl, and optionally substituted loweralkyl, cycloloweralkyl, cyclicaminoalkyl, alkylaminoalkyl, loweralkoxy, amino, alkylamino, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, aryl and heteroaryl;

R<sub>5</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, and optionally substituted loweralkyl, cycloalkyl, alkoxy, amino, aminoalkoxy, carbonyloxy, aminocarbonyloxy, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, heteroaralkylcarbonylamino, cycloimido, heterocycloimido, amidino, cycloamidino, heterocycloamidino, guanidinyl, aryl, biaryl, heteroaryl, heteroarylaryl, heteroarylheteroaryl, heterocycloalkyl, heterocyclo-carbonyloxy, heteroarylcarbonyloxy, and arylsulfonamido;

R<sub>6</sub> is selected from the group consisting of hydrogen, and optionally substituted aryl, heteroaryl, and heterocylo;

R<sub>7</sub> is selected from the group consisting of hydrogen, hydroxy, halo, carboxyl, nitro, amino, amido, amidino, imido, cyano, sulfonyl, methanesulfonyl, and substituted or unsubstituted alkyl, alkoxy, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, heteroarylcarbonyloxy, heteroaralkylcarbonyloxy, alkylaminocarbonyloxy, arylaminocarbonyloxy, formyl, loweralkylcarbonyl, loweralkoxycarbonyl, aminocarbonyl, aminoaryl, alkylsulfonyl, sulfonamido, aminoalkoxy, alkylamino, heteroarylamino, alkylcarbonylamino, alkylaminocarbonylamino, arylaminocarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino cycloamido, cyclothioamido, cycloamidino, heterocycloamidino, cycloalkyl, cycloimido, heterocycloimido, guanidiny, aryl, heteroaryl, heterocyclo, heterocycloalkyl, arylsulfonyl and arylsulfonamido;

the tautomers thereof;

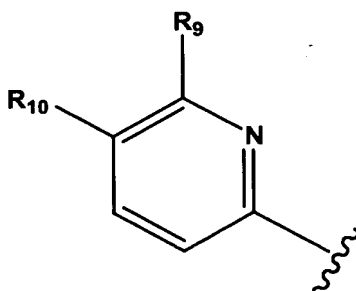
or a pharmaceutically acceptable salt thereof.

2. A compound of claim 1 wherein X is nitrogen.

3. A compound of claim 1 wherein R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> are hydrogen and R<sub>4</sub> is selected from the group consisting of hydrogen, methyl, ethyl, aminoethyl, dimethylaminoethyl, pyridylethyl, piperidiny, pyrrolidinyethyl, piperazinyethyl and morpholinyethyl.

4. A compound of claim 1 wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>, are hydrogen.

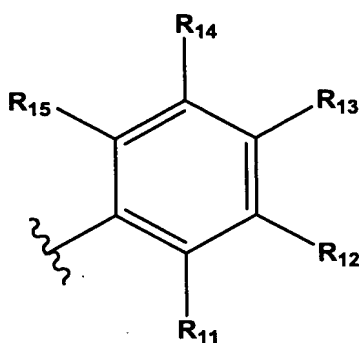
5. A compound of claim 1 wherein A<sub>1</sub> has the formula:



(IV)

wherein R<sub>9</sub> and R<sub>10</sub> are independently selected from the group consisting of hydrogen, hydroxy, nitro, amino, cyano, halo, thioamido, amidino, oxamidino, alkoxyamidino, imidino, guanidiny, sulfonamido, carboxyl, formyl, loweralkyl, aminoloweralkyl, loweralkylaminoloweralkyl, haloloweralkyl, loweralkoxy, haloloweralkoxy, loweralkoxyalkyl, loweralkylaminoloweralkoxy, loweralkylcarbonyl, loweraralkylcarbonyl, lowerheteroaralkylcarbonyl, alkylthio, aryl and, aralkyl.

6. A compound of claim 1 wherein at least one of R<sub>5</sub> and R<sub>8</sub> is a substituted or unsubstituted moiety of the formula:



(V)

wherein R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, and R<sub>15</sub> are independently selected from the group consisting of hydrogen, nitro, amino, cyano, halo, thioamido, carboxyl, hydroxy, and optionally substituted loweralkyl, loweralkoxy, loweralkoxyalkyl, haloloweralkyl, haloloweralkoxy, aminoalkyl, alkylamino, aminoalkylalkynyl, alkylaminoalkylalkynyl, alkylthio, alkylcarbonylamino, aralkylcarbonylamino, heteroaralkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino aminocarbonyl, loweralkylaminocarbonyl, aminoaralkyl, loweralkylaminoalkyl, aryl, heteroaryl, cycloheteroalkyl, aralkyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, arylcarbonyloxyalkyl, alkylcarbonyloxyalkyl, heteroarylcarbonyloxyalkyl, aralkylcarbonyloxyalkyl, and heteroaralkylcarbonyloxyalkyl.

7. A compound of claim 6 wherein R<sub>11</sub>, R<sub>12</sub>, R<sub>14</sub> and R<sub>15</sub> are hydrogen and R<sub>13</sub> is selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl, aminocarbonyl, alkylaminocarbonyl and cyano.

8. A compound of claim 6 wherein  $R_{11}$ ,  $R_{13}$ , and  $R_{15}$  are hydrogen and  $R_{12}$  and  $R_{14}$  are independently selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl and cyano.

9. A compound of claim 6 wherein  $R_{11}$ ,  $R_{12}$ ,  $R_{14}$ , and  $R_{15}$  are hydrogen and  $R_{13}$  is heteroaryl.

10. A compound of claim 6 wherein  $R_{11}$ ,  $R_{12}$ ,  $R_{14}$ , and  $R_{15}$  are hydrogen and  $R_{13}$  is a heterocycloalkyl.

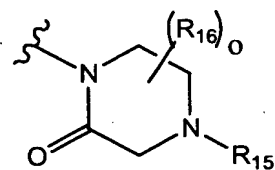
11. A compound of claim 6 wherein at least one of  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$ , and  $R_{15}$  are halo and the remainder of  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$ , and  $R_{15}$  are hydrogen.

12. A compound of claim 1 wherein at least one of  $R_5$  and  $R_8$  is selected from the group consisting of dichlorophenyl, difluorophenyl, trifluoromethylphenyl, chlorofluorophenyl, bromochlorophenyl, ethylphenyl, methylchlorophenyl, imidazolylphenyl, cyanophenyl, morphlinophenyl and cyanochlorophenyl.

13. A compound of claim 1 wherein  $R_6$  is substituted or unsubstituted aryl or heteroaryl.

14. A compound of claim 1 wherein  $R_6$  is substituted or unsubstituted pyridyl, pyrimidinyl, piperazinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thienyl, furanyl, quinolinyl, pyrrolylpyridyl, benzothiazolyl, benzopyridyl, benzotriazolyl, and benzimidazolyl.

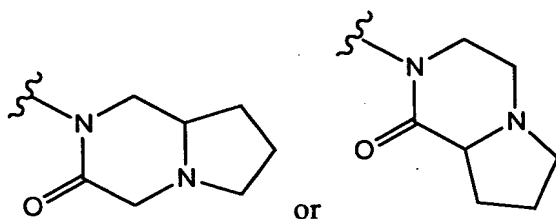
15. A compound of claim 1 wherein  $R_6$  is a monoketopiperazinyl group having the structure:



wherein  $R_{15}$  and  $R_{16}$  are independently selected from the group consisting of hydrogen, loweralkyl, loweralkynyl, aryl, heteroaryl, arylloweralkyl, loweralkylarylloweralkyl, haloloweralkyl, haloarylloweralkyl carbocyclic and

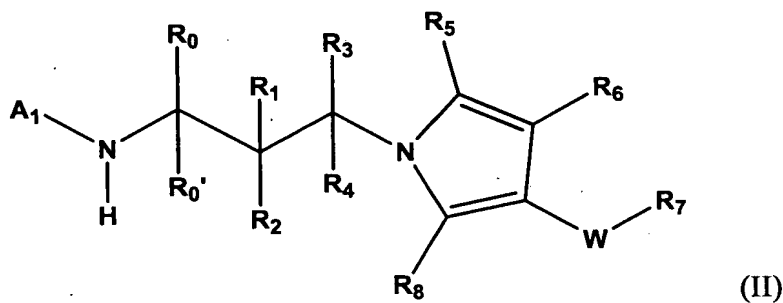
heterocyclic; or  $R_8$  can be taken with another  $R_{16}$  or with  $R_{15}$  to form a carbocyclic, heterocyclic or aryl ring; and  $o$  is an integer between 1 and 6.

16. A compound of claim 15 wherein  $R_{15}$  is loweralkyl, such as methyl, ethyl, n-propyl, isopropyl, cyclopropyl, n-butyl, iso-butyl or t-butyl, or  $R_{15}$  is taken with  $R_{16}$  to form a group having the structure:



17. A compound in claim 1 wherein  $R_5$  and  $R_8$  are independently hydrogen or lower alkyl.

18. A compound having the structure:



wherein:

W is absent or is selected from the group consisting of  $-O-$ ,  $-S-$ ,  $-S(O)-$ ,  $-SO_2-$ ,  $-NH-$ ,  $-NH-CO-$ ,  $-NR'CO-$ ,  $-NHSO_2-$ ,  $-NR'SO_2-$ ,  $-CO-$ ,  $-CO_2-$ ,  $-CH_2-$ ,  $-CF_2-$ ,  $-CHF$ ,  $-CONH-$ ,  $-CONR'-$ , and  $-NR'-$ , where  $R'$  is alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, heterocyclo;

$A_1$  is optionally substituted aryl, heteroaryl, or a protecting group;

$R_0$  and  $R_0'$  are independently selected from the group consisting of hydrogen and methyl;

$R_1$ ,  $R_2$ ,  $R_3$ , and  $R_4$  are independently selected from the group consisting of hydrogen, hydroxyl, and optionally substituted loweralkyl, cycloloweralkyl, cyclicaminoalkyl, alkylaminoalkyl, loweralkoxy, amino, alkylamino, alkylcarbonyl,

arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, aryl and heteroaryl;

R<sub>5</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, and optionally substituted loweralkyl, cycloalkyl, alkoxy, amino, aminoalkoxy, carbonyloxy, aminocarbonyloxy, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, heteroaralkylcarbonylamino, cycloimido, heterocycloimido, amidino, cycloamidino, heterocycloamidino, guanidinyl, aryl, biaryl, heteroaryl, heteroarylaryl, heteroarylheteroaryl, heterocycloalkyl, heterocyclocarbonyloxy, heteroarylcarbonyloxy, and arylsulfonamido;

R<sub>6</sub> is selected from the group consisting of hydrogen, and optionally substituted aryl, heteroaryl, and heterocylo;

R<sub>7</sub> is selected from the group consisting of hydrogen, hydroxy, halo, carboxyl, nitro, amino, amido, amidino, imido, cyano, sulfonyl, methanesulfonyl, and substituted or unsubstituted alkyl, alkoxy, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, heteroarylcarbonyloxy, heteroaralkylcarbonyloxy, alkylaminocarbonyloxy, arylaminocarbonyloxy, formyl, loweralkylcarbonyl, loweralkoxycarbonyl, aminocarbonyl, aminoaryl, alkylsulfonyl, sulfonamido, aminoalkoxy, alkylamino, heteroarylamino, alkylcarbonylamino, alkylaminocarbonylamino, arylaminocarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, cycloamido, cyclothioamido, cycloamidino, heterocycloamidino, cycloalkyl, cycloimido, heterocycloimido, guanidinyl, aryl, heteroaryl, heterocyclo, heterocycloalkyl, arylsulfonyl and arylsulfonamido;

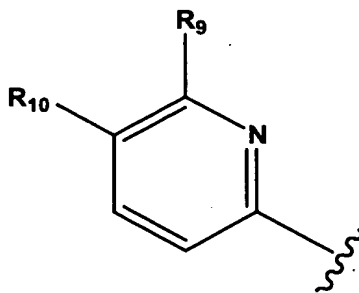
the tautomers thereof;

or a pharmaceutically acceptable salt thereof.

19. A compound of claim 18 wherein R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> are hydrogen and R<sub>4</sub> is selected from the group consisting of hydrogen, methyl, ethyl, aminoethyl, dimethylaminoethyl, pyridylethyl, piperidinyl, pyrrolidinylethyl, piperazinylethyl and morpholinylethyl.

20. A compound of claim 18 wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>, are hydrogen.

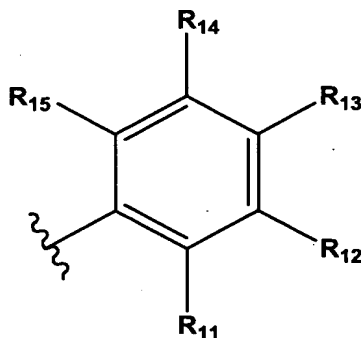
21. A compound of claim 18 wherein A<sub>1</sub> has the formula:



(IV)

wherein R<sub>9</sub> and R<sub>10</sub> are independently selected from the group consisting of hydrogen, hydroxy, nitro, amino, cyano, halo, thioamido, amidino, oxamidino, alkoxyamidino, imidino, guanidinyl, sulfonamido, carboxyl, formyl, loweralkyl, aminoloweralkyl, loweralkylaminoloweralkyl, haloloweralkyl, loweralkoxy, haloloweralkoxy, loweralkoxyalkyl, loweralkylaminoloweralkoxy, loweralkylcarbonyl, loweraralkylcarbonyl, lowerheteroaralkylcarbonyl, alkylthio, aryl and, aralkyl.

22. A compound of claim 18 wherein at least one of R<sub>5</sub> and R<sub>8</sub> is a substituted or unsubstituted moiety of the formula:



(V)

wherein R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, and R<sub>15</sub> are independently selected from the group consisting of hydrogen, nitro, amino, cyano, halo, thioamido, carboxyl, hydroxy, and optionally substituted loweralkyl, loweralkoxy, loweralkoxyalkyl, haloloweralkyl, haloloweralkoxy, aminoalkyl, alkylamino, aminoalkylalkynyl, alkylaminoalkylalkynyl, alkylthio, alkylcarbonylamino, aralkylcarbonylamino, heteroaralkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino aminocarbonyl, loweralkylaminocarbonyl, aminoaralkyl, loweralkylaminoalkyl, aryl, heteroaryl, cycloheteroalkyl, aralkyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, arylcarbonyloxyalkyl,

alkylcarbonyloxyalkyl, heteroarylcarbonyloxyalkyl, aralkylcarbonyloxyalkyl, and heteroaralkcarbonyloxyalkyl.

23. A compound of claim 22 wherein  $R_{11}$ ,  $R_{12}$ ,  $R_{14}$  and  $R_{15}$  are hydrogen and  $R_{13}$  is selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl, aminocarbonyl, alkylaminocarbonyl and cyano.

24. A compound of claim 22 wherein  $R_{11}$ ,  $R_{13}$ , and  $R_{15}$  are hydrogen and  $R_{12}$  and  $R_{14}$  are independently selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl and cyano.

25. A compound of claim 22 wherein  $R_{11}$ ,  $R_{12}$ ,  $R_{14}$ , and  $R_{15}$  are hydrogen and  $R_{13}$  is heteroaryl.

26. A compound of claim 22 wherein  $R_{11}$ ,  $R_{12}$ ,  $R_{14}$ , and  $R_{15}$  are hydrogen and  $R_{13}$  is a heterocycloalkyl.

27. A compound of claim 22 wherein at least one of  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$ , and  $R_{15}$  are halo and the remainder of  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$ , and  $R_{15}$  are hydrogen.

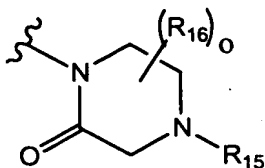
28. A compound of claim 18 wherein at least one of  $R_5$  and  $R_8$  is selected from the group consisting of dichlorophenyl, difluorophenyl, trifluoromethylphenyl, chlorofluorophenyl, bromochlorophenyl, ethylphenyl, methylchlorophenyl, imidazolylphenyl, cyanophenyl, morpholinophenyl and cyanochlorophenyl.

29. A compound of claim 18 wherein  $R_6$  is substituted or unsubstituted aryl or heteroaryl.

30. A compound of claim 18 wherein  $R_6$  is substituted or unsubstituted pyridyl, pyrimidinyl, piperazinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thienyl, furanyl, quinolinyl, pyrrolylpyridyl, benzothiazolyl, benzopyridyl, benzotriazolyl, and benzimidazolyl.

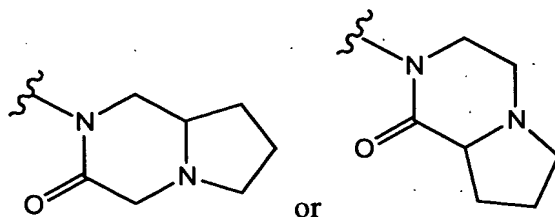
31. A compound of claim 18 wherein  $R_6$  is a monoketopiperazinyl group having the structure:





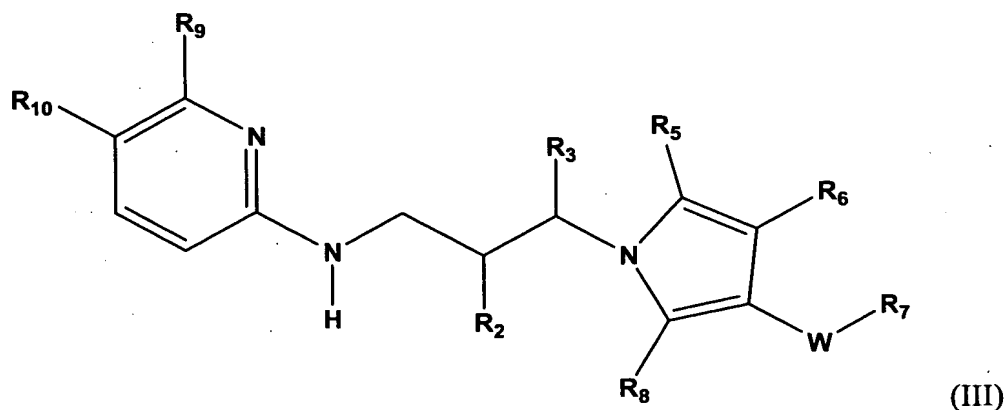
wherein  $R_{15}$  and  $R_{16}$  are independently selected from the group consisting of hydrogen, loweralkyl, loweralkynyl, aryl, heteroaryl, arylloweralkyl, loweralkylarylloweralkyl, haloloweralkyl, haloarylloweralkyl carbocyclic and heterocyclic; or  $R_8$  can be taken with another  $R_{16}$  or with  $R_{15}$  to form a carbocyclic, heterocyclic or aryl ring; and  $o$  is an integer between 1 and 6.

32. A compound of claim 31 wherein  $R_{15}$  is loweralkyl, or  $R_{15}$  is taken with  $R_{16}$  to form a group having the structure:



33. A compound in claim 18 wherein  $R_5$  and  $R_8$  are independently hydrogen or lower alkyl.

34. A compound having the structure:



wherein  $W$  is absent or is selected from the group consisting of  $-O-$ ,  $-S-$ ,  $-S(O)-$ ,  $-SO_2-$ ,  $-NH-$ ,  $-NH-CO-$ ,  $-NR'CO-$ ,  $-NHSO_2-$ ,  $-NR'SO_2-$ ,  $-CO-$ ,  $-CO_2-$ ,  $-CH_2-$ ,  $-CF_2-$ ,

CHF, -CONH-, -CONR'-, and -NR'-, where R' is alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, heterocyclo;

R<sub>2</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, hydroxyl, and optionally substituted loweralkyl, cycloloweralkyl, cyclicaminoalkyl, alkylaminoalkyl, loweralkoxy, amino, alkylamino, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, aryl and heteroaryl;

R<sub>5</sub> and R<sub>8</sub> are independently selected from the group consisting of hydrogen, halo, and optionally substituted loweralkyl, cycloalkyl, alkoxy, amino, aminoalkoxy, carbonyloxy, aminocarbonyloxy, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, heteroaralkylcarbonylamino, cycloimido, heterocycloimido, amidino, cycloamidino, heterocycloamidino, guanidiny, aryl, biaryl, heteroaryl, heteroarylaryl, heteroarylheteroaryl, heterocycloalkyl, heterocyclocarbonyloxy, heteroarylcarbonyloxy, and arylsulfonamido;

R<sub>6</sub> is selected from the group consisting of hydrogen, and optionally substituted aryl, heteroaryl, and heterocyclo;

R<sub>7</sub> is selected from the group consisting of hydrogen, hydroxy, halo, carboxyl, nitro, amino, amido, amidino, imido, cyano, sulfonyl, methanesulfonyl, and substituted or unsubstituted alkyl, alkoxy, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, heteroarylcarbonyloxy, heteroaralkylcarbonyloxy, alkylaminocarbonyloxy, arylaminocarbonyloxy, formyl, loweralkylcarbonyl, loweralkoxycarbonyl, aminocarbonyl, aminoaryl, alkylsulfonyl, sulfonamido, aminoalkoxy, alkylamino, heteroaryl-amino, alkylcarbonylamino, alkylaminocarbonylamino, arylaminocarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino cycloamido, cyclothioamido, cycloamidino, heterocycloamidino, cycloalkyl, cycloimido, heterocycloimido, guanidiny, aryl, heteroaryl, heterocyclo, heterocycloalkyl, arylsulfonyl and arylsulfonamido;

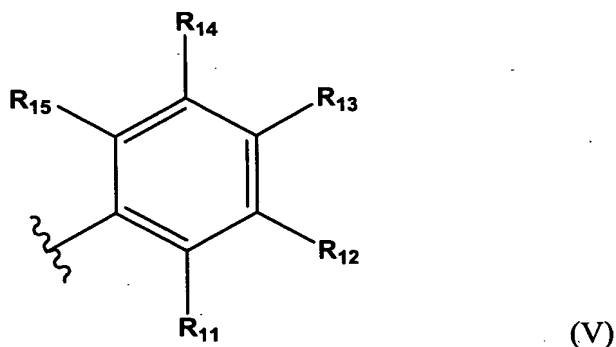
R<sub>9</sub> and R<sub>10</sub> are independently selected from the group consisting of hydrogen, hydroxy, nitro, amino, cyano, halo, thioamido, amidino, oxamidino, alkoxyamidino, imidino, guanidiny, sulfonamido, carboxyl, formyl, loweralkyl, aminoloweralkyl, loweralkylaminoloweralkyl, haloloweralkyl, loweralkoxy, haloloweralkoxy, loweralkoxyalkyl, loweralkylaminoloweralkoxy, loweralkylcarbonyl, loweraralkyl-

carbonyl, lowerheteroaralkylcarbonyl, alkylthio, aryl and, aralkyl. Most preferably, A is selected from the group consisting of aminopyridyl, nitropyridyl, aminonitropyridyl, cyanopyridyl, cyanothiazolyl, aminocyanopyridyl, trifluoromethylpyridyl, methoxypyridyl, methoxynitropyridyl, methoxycyanopyridyl and nitrothiazolyl; the tautomers thereof; or a pharmaceutically acceptable salt thereof.

35. A compound of claim 34 wherein R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> are hydrogen and R<sub>4</sub> is selected from the group consisting of hydrogen, methyl, ethyl, aminoethyl, dimethylaminoethyl, pyridylethyl, piperidinyl, pyrrolidinylethyl, piperazinylethyl and morpholinylethyl.

36. A compound of claim 34 wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>, are hydrogen.

37. A compound of claim 34 wherein at least one of R<sub>5</sub> and R<sub>7</sub> is a substituted or unsubstituted moiety of the formula:



wherein R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, and R<sub>15</sub> are independently selected from the group consisting of hydrogen, nitro, amino, cyano, halo, thioamido, carboxyl, hydroxy, and optionally substituted loweralkyl, loweralkoxy, loweralkoxyalkyl, haloloweralkyl, haloloweralkoxy, aminoalkyl, alkylamino, aminoalkylalkynyl, alkylaminoalkylalkynyl, alkylthio, alkylcarbonylamino, aralkylcarbonylamino, heteroaralkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino aminocarbonyl, loweralkylaminocarbonyl, aminoaralkyl, loweralkylaminoalkyl, aryl, heteroaryl, cycloheteroalkyl, aralkyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, arylcarbonyloxyalkyl, alkylcarbonyloxyalkyl, heteroarylcarbonyloxyalkyl, aralkylcarbonyloxyalkyl, and heteroaralkylcarbonyloxyalkyl.

38. A compound of claim 37 wherein  $R_{11}$ ,  $R_{12}$ ,  $R_{14}$  and  $R_{15}$  are hydrogen and  $R_{13}$  is selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl, aminocarbonyl, alkylaminocarbonyl and cyano.

39. A compound of claim 37 wherein  $R_{11}$ ,  $R_{13}$ , and  $R_{15}$  are hydrogen and  $R_{12}$  and  $R_{14}$  are independently selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl and cyano.

40. A compound of claim 37 wherein  $R_{11}$ ,  $R_{12}$ ,  $R_{14}$ , and  $R_{15}$  are hydrogen and  $R_{13}$  is heteroaryl.

41. A compound of claim 37 wherein  $R_{11}$ ,  $R_{12}$ ,  $R_{14}$ , and  $R_{15}$  are hydrogen and  $R_{13}$  is a heterocycloalkyl.

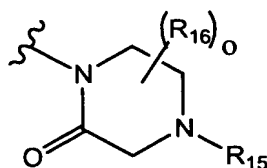
42. A compound of claim 37 wherein at least one of  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$ , and  $R_{15}$  are halo and the remainder of  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$ , and  $R_{15}$  are hydrogen.

43. A compound of claim 34 wherein at least one of  $R_5$  and  $R_8$  is selected from the group consisting of dichlorophenyl, difluorophenyl, trifluoromethylphenyl, chlorofluorophenyl, bromochlorophenyl, ethylphenyl, methylchlorophenyl, imidazolylphenyl, cyanophenyl, morpholinophenyl and cyanochlorophenyl.

44. A compound of claim 34 wherein  $R_6$  is substituted or unsubstituted aryl or heteroaryl.

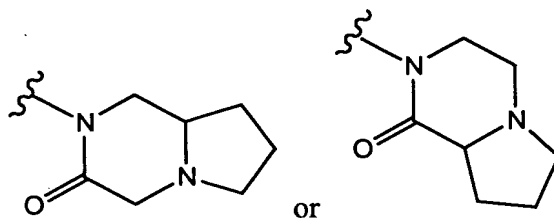
45. A compound of claim 34 wherein  $R_6$  is substituted or unsubstituted pyridyl, pyrimidinyl, piperazinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thienyl, furanyl, quinolinyl, pyrrolypyridyl, benzothiazolyl, benzopyridyl, benzotriazolyl, and benzimidazolyl.

46. A compound of claim 34 wherein  $R_6$  is a monoketopiperazinyl group having the structure:



wherein  $R_{15}$  and  $R_{16}$  are independently selected from the group consisting of hydrogen, loweralkyl, loweralkynyl, aryl, heteroaryl, arylloweralkyl, loweralkylarylloweralkyl, haloloweralkyl, haloarylloweralkyl carbocyclic and heterocyclic; or  $R_8$  can be taken with another  $R_{16}$  or with  $R_{15}$  to form a carbocyclic, heterocyclic or aryl ring; and  $o$  is an integer between 1 and 6.

47. A compound of claim 46 wherein  $R_{15}$  is loweralkyl, or  $R_{15}$  is taken with  $R_{16}$  to form a group having the structure:



48. A compound in claim 34 wherein  $R_5$  and  $R_8$  are independently hydrogen or lower alkyl.

49. A composition comprising an amount of a compound of claim 1 effective to inhibit GSK3 activity in a human or animal subject when administered thereto, together with a pharmaceutically acceptable carrier.

50. A composition comprising an amount of a compound of claim 18 effective to inhibit GSK3 activity in a human or animal subject when administered thereto, together with a pharmaceutically acceptable carrier.

51. A composition comprising an amount of a compound of claim 34 effective to inhibit GSK3 activity in a human or animal subject when administered thereto, together with a pharmaceutically acceptable carrier.

52. A method of inhibiting GSK3 activity in a human or animal subject, comprising administering to the human or animal subject a composition of claim 49.

53. A method of inhibiting GSK3 activity in a human or animal subject, comprising administering to the human or animal subject a composition of claim 50.

54. A method of inhibiting GSK3 activity in a human or animal subject, comprising administering to the human or animal subject a composition of claim 51.

55. A method of treating a cell comprising administering to the cell an amount of a compound of claim 1 effective to inhibit GSK3 activity in the cell.

56. A method of treating a cell comprising administering to the cell an amount of a compound of claim 18 effective to inhibit GSK3 activity in the cell.

57. A method of treating a cell comprising administering to the cell an amount of a compound of claim 34 effective to inhibit GSK3 activity in the cell.

58. A method for treating a GSK3-mediated disorder in a human or animal subject, comprising administering to the human or animal subject an amount of a compound of claim 1 effective to inhibit GSK3 activity in the subject.

59. A method of claim 58, wherein the composition is administered by a mode of administration selected from the group consisting of oral, subcutaneous, transdermal, transmucosal, iontophoretic, intravenous, intrathecal, buccal, sublingual, intranasal, and rectal administration.

60. A method of claim 58, wherein said GSK3-mediated disorder is selected from the group consisting of diabetes, Alzheimer's disease, obesity, atherosclerotic cardiovascular disease, essential hypertension, polycystic ovary syndrome, syndrome X, ischemia, traumatic brain injury, bipolar disorder, immunodeficiency and cancer.

61. A method of claim 58, which further comprises administering to the subject one or more additional active agents.

62. A method of claim 58, wherein the GSK3-mediated disorder is diabetes and the additional active agent is selected from the group consisting of insulin, troglitazone, rosiglitazone, pioglitazone, glipizide and metformin.

63. A method for treating a human or animal subject, comprising administering to the human or animal subject an amount of a compound of claim 1 effective to inhibit tau phosphorylation in the subject.

64. The method of claim 63 wherein the compound is 1-{3-[(6-amino-5-nitropyridin-2-yl)amino]propyl}-4-(2,4-dichlorophenyl)-N-[(1S)-2-hydroxy-1-methylethyl]-1H-pyrrole-3-carboxamide.

65. A compound of claim 1, 18 or 34 for use as a pharmaceutical.

66. Use of a compound of claim 1, 18 or 34 in the manufacture of a medicament for the inhibition of GSK3 activity in a human or animal subject.

67. Use of a compound of claim 1, 18 or 34 in the manufacture of a medicament for the treatment of diabetes, Alzheimer's disease and other neurodegenerative disorders, obesity, atherosclerotic cardiovascular disease, essential hypertension, polycystic ovary syndrome, syndrome X, ischemia, traumatic brain injury, bipolar disorder or cancer.

68. Use of a compound of claim 1, 18 or 34 in the manufacture of a medicament for the inhibition of tau phosphorylation.

69. The use of claim 68 wherein the compound is 1-{3-[(6-amino-5-nitropyridin-2-yl)amino]propyl}-4-(2,4-dichlorophenyl)-N-[(1S)-2-hydroxy-1-methylethyl]-1H-pyrrole-3-carboxamide.